COMPARISON OF MODIFIED DISCRIMINANT FUNCTION AND GLASGOW ALCOHOLIC HEPATITIS SCORE IN PREDICTING ONE MONTH MORTALITY

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CHENNAI

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CERTIFICATE

This is to certify that this dissertation titled

"COMPARISON OF MODIFIED DISCRIMINANT FUNCTION AND GLASGOW ALCOHOLIC HEPATITIS SCORE IN PREDICTING ONE MONTH MORTALITY"

is the bonafide work done by **Dr. RENGARAJ G,** Post Graduate Student (2010 – 2013) in the Department of General medicine , Govt. Stanley Medical College and Hospital, Chennai under the direct guidance and supervision and in partial fulfilment of the regulations laid down by The Tamil Nadu Dr. M.G.R. Medical University, Chennai for M.D. Branch I, General Medicine Degree Examination to be held in April 2013.

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I, **Dr. RENGARAJ . G.,** solemnly declare that the dissertation titled

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is a bonafide work done by me at Govt. Stanley Medical College and Hospital from march 2012 to august 2012 under the guidance and supervision of my unit chief,

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Dr .Rengaraj.G

CONTENTS

ABBREVIATIONS

GAHS	-	Glasgow alcoholic hepatitis score
mDF	-	modified discriminant function
MELD	-	Model for end-stage liver disease
ADH	-	alcohol dehydrogenase
ALDH	-	aldehyde dehydrogenase
TNF	-	tumour necrosis factor
IL	-	interleukin
IFN	-	interferon
TGF	-	transforming growth factor
AST	-	aspartate transaminase
ALT	-	alanine transaminase
ALP	-	alkaline phosphatase
GGT	-	gamma glutamyl transpeptidase
AUDIT	-	alcohol use disorder identification test
NASH	-	non-alcoholic steatohepatitis
PT	-	prothrombin time
INR	-	international normalized ratio

INTRODUCTION

INTRODUCTION

HISTORY:

Alcohol consumption has been prevalent as early as 10000 B.C.- Beer mugs belonging to the Neolithic period(late stone age) shows the fact that fermentation was intentionally done at that time. These earliest beverages are made from berries and honey.

The detailed process of brewing dates back to 2000 B.C. in ancient Egypt at the dawn of civilisation. In ancient Egypt, alcoholic beverages were considered very important. In fact, Egyptians had a god of wine, Osiris and Osiris was worshipped in the entire country. They had a belief that Osiris invented beer. Beer was brewed and used in home daily. Alcohol was offered to gods during religious ceremonies. They clearly had limitations in the amount to be consumed and the majority who used it , drunk moderately.

Ancient Chinese believed alcohol to be a spiritual food. It was used in moderation during festivals, religious ceremonies, offering rituals, executions, marriage, death, battles and celebration of victories. It was one of the main source of income to the treasury.

Greeks had a set of rules for drinking like moderate drinking, diluting wine with water and avoiding excess consumption. Except during the Dionysus cult- which believed intoxication will bring people close to god, majority of Greeks upheld the idea of moderation. But Macedonians viewed drunkenness as a symbol of masculinity. when Hebrews were exposed to alcohol they started using it widely and it even became a part of their religious ceremonies like regular wine drinking outside jewish temples

Early Romanians used wine in moderation. But later half of their period was associated with heavy drinking. In india, alcohol dates back to 3000 B.C – 2000 B.C, during the period of Indus valley civilisation. A drink called sura made from fermented wheat, sugarcane and grapes was drunk by kshatriyas. Ayurveda texts shows that beneficial effects of alcohol if used in moderate amount and harmful effects if consumed in excess.

By first century B.C. misuse of alcohol became prevalent and intoxication occurred with increased frequency

With the rise of Christianity by fourth and fifth century A.D. alcohol was considered god's gift, but excess alcohol consumption leading to drunkenness was considered as a sin. In the medieval period, the first clear evidence of alcohol distillation occurred at Greece.
By 15^{th} and 16^{th} century, germans mastered the art of distillation. Some people increased their consumption dramatically because of the belief that distilled beverages protected them against black death and plague.

In the modern period, consumption increased gradually. This is the period during which many varieties of alcohol like champagne, rum, gin, ale, etc started to emerge. The increased consumption lead to gin epidemic in England by 17^{th} century. Hence , legislation was passed to limit the sale of gin which curbed the rise in consumption. Alcohol production industry became lucrative.

Thus alcohol, which was initially consumed as a part of religious ceremonies was later consumed in moderation for pleasure. Then, people started

consuming alcohol to intoxicating levels. Initially the usage was confined to elite people. Later on, with the advent of industrialisation , alcohol production increased and it became available to all groups irrespective of their economy. This lead to increased consumption of alcohol among widespread groups of People and the alcohol related diseases started to emerge.

PRESENT SCENARIO IN INDIA :

Alcohol is the most frequently used drug worldwide and is considered a socially acceptable hepatotoxin.

*About 30 – 35 % of adult males and 5% adult females consume alcohol. The male: female ratio was 6 : 1

*The average age of initiating alcohol is 17 years. in 1980, this was at 28 years. The consumption starts in social circles on experimental basis and then becomes addictive.

* The chances of addiction are increased when drinking was started at a younger age.

* the incidence is high in age group of 41 – 50 years and people with lower education status

*The average duration of consumption is more than 10 years**.** the amount drunk increases with age.

* the legal age for drinking varies between 18 to 25 depending on the state

*IMFL(Indian made foreign liquor) and Beer is the most preferred among youngsters, brandy and rum among people in rural regions

*usage is high in goa, north-eastern and southern states

*revenue related to taxation from liquor industry is one of the major sources of income to the government

*only half of the consumption is documented.

*half of the drinkers come under the category of hazardous drinking

* the documentation of hazardous consequences of alcohol was not done Properly

* alcoholics have higher morbidity, hospitalisation and mortality

* alcohol is involved in 20 -30 % of road traffic accidents

* increased association with HIV and other sexually transmitted diseases

*it is a co-morbid factor for psychiatric illnesses

* Higher Cardiovascular morbidity among alcoholics

*violence and abuse of women and children are linked with alcoholism

*increasing crime rates have been linked with alcohol.

*prohibition of alcohol didn't had an effect on consumption. Instead, smuggling and illegal consumption increased

* alcoholics feel guilty because of their drinking and this prevents them from seeking medical care

*alcoholism leads to the loss of economy by two ways – one, due to the money spent on alcohol and two, the resources spent on managing alcohol related injuries, accidents and medical illnesses

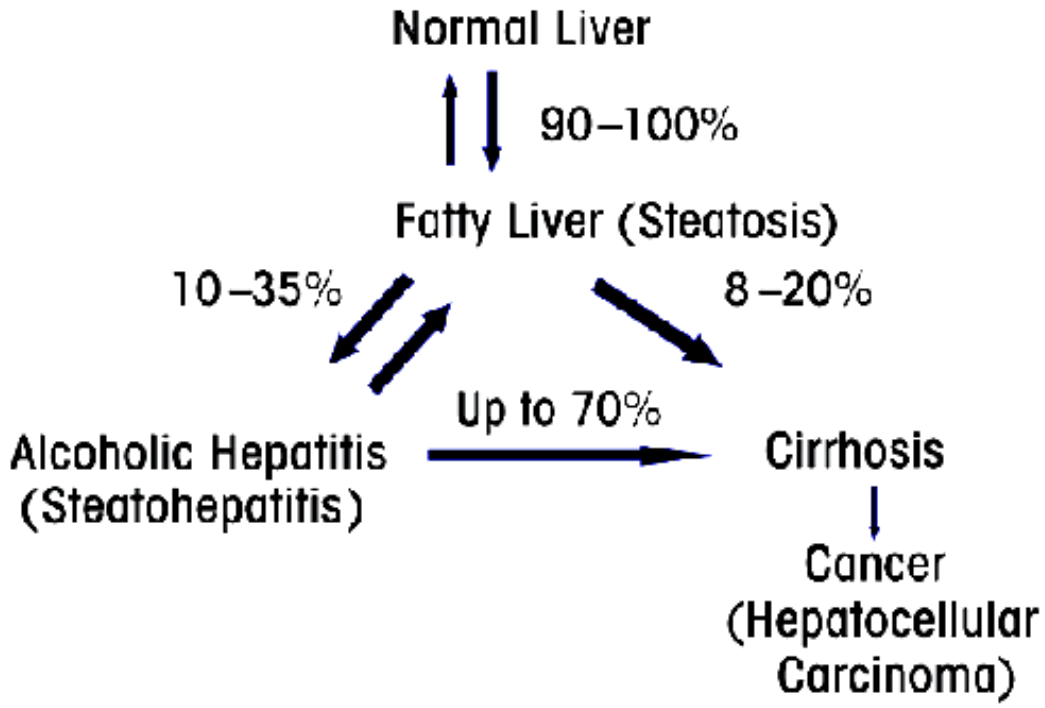
The emerging trends are

- social drinking was considered as a part of life style
- Initiation at earlier, younger age
- Increasing consumption among females
- Higher consumption among sub-urban and rural areas
- Preference for drinks with high alcohol content

The need of the hour is a scientific and a rational alcohol control policy.

ALCOHOLIC LIVER DISEASE:

Alcoholic liver disease (ALD) includes a wide range of injury, from reversible Steatohepatitis to irreversible cirrhosis. Alcohol is a common cause of liver disease worldwide. Pathologically, the varied manifestations of the disease are shown below:



Among these, alcoholic hepatitis is a very important entity because , severe alcoholic hepatitis is associated with very high short-term mortality rates. So far, the severity is identified by calculating modified Discriminant function. m DF greater than or equal to 32 is considered severe and treated

with steroids or pentoxifylline . Thus it is important for an accurate scoring system to identify and treat the severe patients.

The mDF includes only PT and bilirubin in calculating the severity of Alcoholic hepatitis. But the presence of renal involvement indicates severe disease with a short-term mortality rate of 75%[1].

Also, in alcoholic hepatitis the inflammatory mechanisms play an important role in pathogenesis, which is why the steroids are being used as treatment. The importance of renal involvement or inflammation in determining the severity of disease is not estimated in mDF score.

Hence there is a need for a new scoring system which can involve the renal function and inflammation. The Glasgow Alcoholic Hepatitis Score involves age, White cell count, urea, PT and bilirubin in calculating the prognosis of alcoholic hepatitis and identifying the patients in need of drug therapy. Since it involves markers for renal dysfunction and inflammation , it can be more accurate than mDF .

Hence, it sounds worthy for me to take up this comparative study of prediction of 1 month mortality in alcoholic hepatitis by mDF and GAHS

AIMS AND OBJECTIVES

AIMS AND OBJECTIVES

1] To estimate the 1 month mortality in alcoholic hepatitis by using mDF and GAHS Score

2] To assess the accuracy of each scoring system in predicting 1 month Mortality.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

PATHOGENESIS OF ALCOHOL INDUCED LIVER INJURY

ALCOHOL METABOLISM IN LIVER:

The major organ for alcohol metabolism is liver. Ethanol is metabolised by three major enzyme systems:

1] alcohol dehydrogenase[ADH]

2] cytochrome P450 isoenzymes, mainly cytochrome P450 2E1

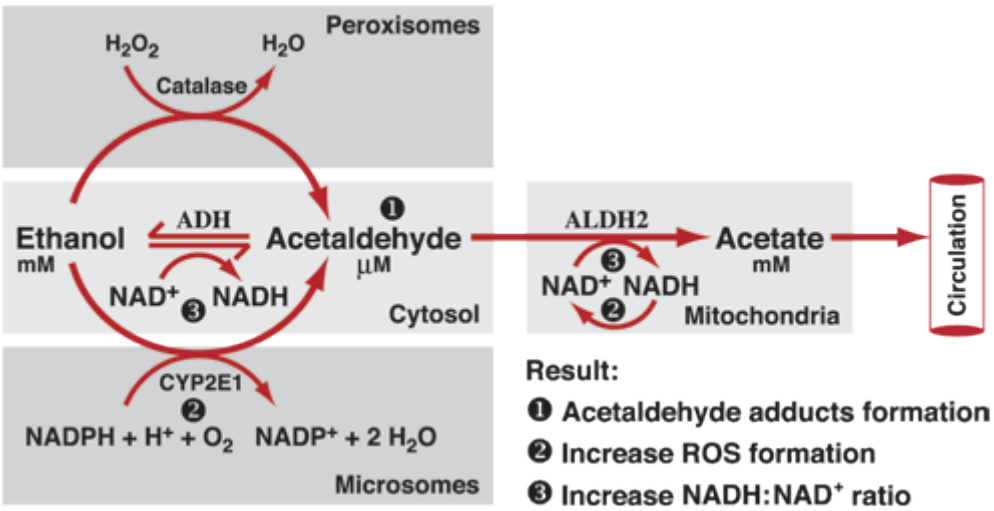
3] Catalase.

Of these, the main enzyme system involved in alcohol metabolism is ALCOHOL DEHYDROGENASE[ADH], located in the cells of the liver[2]. It metabolises 80-85% of ethanol.The Cytochrome P450 isoenzymes, predominantly CYP2E1 is situated in the smooth Endoplasmic Reticulum as a part of microsomal ethanol-oxidising system. This system metabolises ethanol at higher blood concentrations[greater than 10 Mm] and contributes to 10-15% of ethanol metabolism[3]. The catalase enzyme present in peroxisomes is

of minor importance, because it metabolises less than 5% of ethanol in the liver.

Ethanol is converted to acetaldehyde by the above three systems. Acetaldehyde is converted to acetate by aldehyde dehydrogenase[ALDH].

Ethanol $\xrightarrow{\text{ADH}}$ acetaldehyde $\xrightarrow{\text{ALDH}}$ acetate



Polymorphisms in ADH results in different elimination rates in different individuals. Various active isoforms like ADH2 and ADH3 results in rapid metabolism of alcohol. These individuals have lower tolerance of alcohol, but they produce more acetaldehyde rapidly resulting in increased liver injury[3].

The major isoenzyme in aldehyde dehydrogenase is ALD H2. It is the predominant metabolism of aldehyde oxidation .Inactive ALD H2 is found in 50% east Asians resulting in impaired acetaldehyde metabolism causing flushing and tachycardia after alcohol consumption –“ oriental flush syndrome”.

METABOLIC ABNORMALITIES:

The metabolic abnormalities that arise in alcoholic liver disease includes several mechanisms:

1] Acetaldehyde – it is a highly reactive and toxic compound. It forms adducts with proteins and small molecules , thus interfering with normal biologic processes. These modified proteins induces host's immune system and results in auto-immune like mechanisms. This type of injury is specific to alcohol.

2] Shift in ratio of NADH to NAD+ to a more reduced state. This inhibits lactate to pyruvate conversion and fatty acid oxidation, resulting in impaired carbohydrate and lipid metabolism.

3] Oxidative stress – CYP2E1 system leaks electrons to initiate oxidative Stress. Also the increased NADH/NAD+ ratio favours superoxide generation.

IMMUNE AND INFLAMMATORY MECHANISMS:

1] DYSREGULATED CYTOKINE PRODUCTION AND KUPFFER CELL ACTIVATION:

In alcoholic liver disease, the increased intestinal permeability causes frequent endotoxemia. This intestine derived LPS activates reticuloendothelial cells of the liver, thereby stimulating cytokines. Also the reactive oxygen species stimulates proinflammatory cytokine production. The production of immunomodulatory cytokines which counter-act these detrimental effects are decreased.

TNF metabolism is dysregulated. TNF is produced in significantly increased amounts because of the gut-derived endotoxin stimulation. serum TNF concentrations show a strong correlation with disease severity and risk of mortality. The levels of pro-inflammatory cytokines in Serum are increased to alarming levels and the levels often correlate with acute-phase reactants, reduced hepatic function, and poor outcomes. This enhanced cytokine response to a physiologic stimulus such as LPS is termed priming.

Hepatocytes normally are resistant to TNF killing. However, hepatocytes in alcoholic hepatitis are sensitized to TNF killing. Mechanisms for this sensitization include mitochondrial depletion of glutathione, accumulation of SAH, and inhibition of proteosomes, among others. Thus both

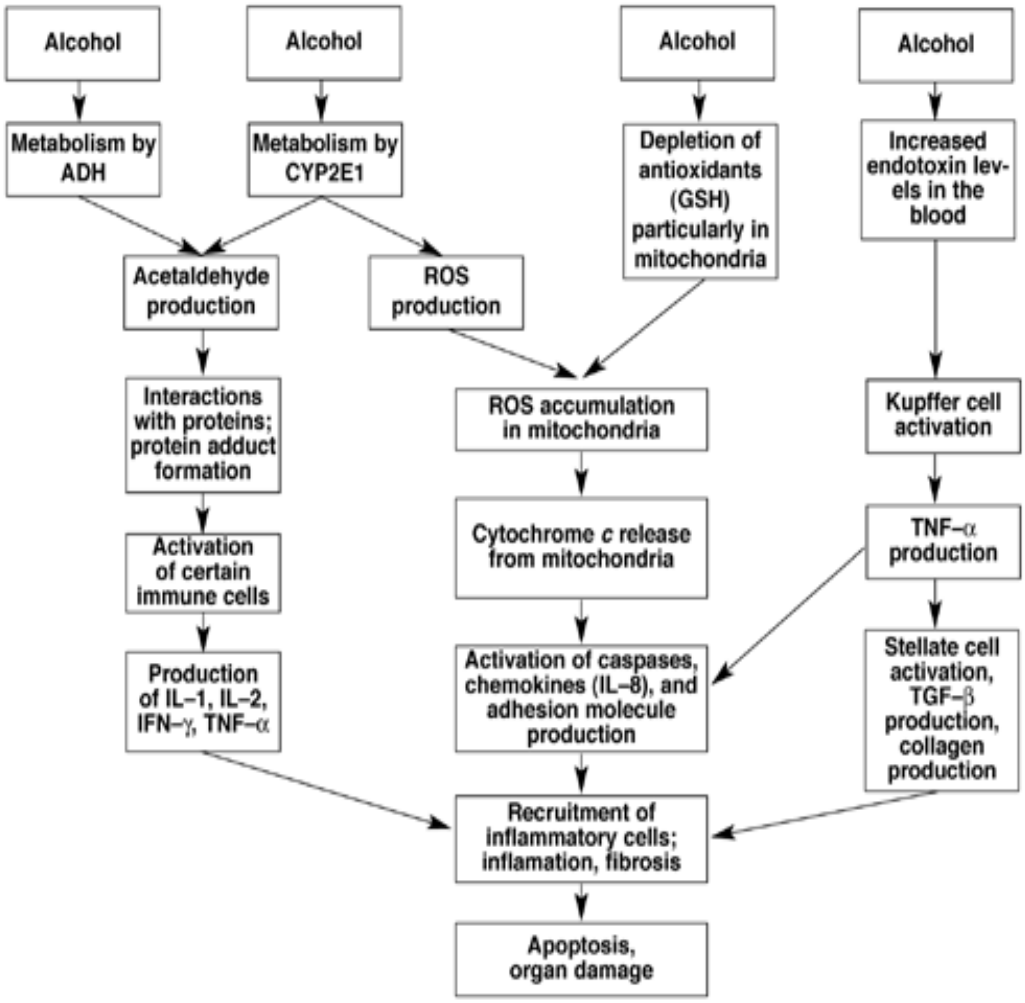
reticuloendothelial cells are primed and hepatocytes are sensitised, resulting in liver damage

2] IMMUNE RESPONSE TO ALTERED HEPATIC PROTEINS:

Alcoholics develop immune or autoimmune response by autoantibodies against phospholipids, heat shock proteins and other antigens[1]. They also develop immune responses against neoantigens generated from the interactions of metabolites of alcohol (e.g., acetaldehyde or hydroxyethyl radicals) with liver proteins. In fact, alcoholic hepatitis may persist histologically for several months after thanol exposure has been stopped.

Role of Cytokines	
Cytokine	**Mechanism**
Pro–inflammatory cytokines	
IL-1	Stimulates inflammation, results in fever
IL–6	Causes B lymphocyte proliferation and antibody production
TNF–α	Stimulates macrophages. Triggers apoptosis and necrosis
TGF–β	Promotes collagen synthesis
Immunoregulatory cytokines	
IL–10	Prevents mitosis in reticuloendothelial cells. it is decreased in alcoholic hepatitis
Chemokines	
IL–8	Attracts PMNs.

Immunological mechanisms in alcohol induced hepatic injury



DIAGNOSIS OF ALCOHOL ABUSE:

Alcohol abuse is defined in an individual who has frequent problems in social, legal, occupational and interpersonal relationships. It can be diagnosed if an individual is consuming alcohol in dangerous situations like driving. It can be defined only when there is no alcohol dependence.

The diagnosis of alcohol abuse can be done using AUDIT-C and the CAGE questionnaire. The denial of patients and inadequate questioning by physicians results in underdiagnosis of patients. The CAGE questionnaire dramatically improves the recognition of patients with problem drinking in primary care clinic.

Table 11. The CAGE Questionnaire.

- Have you ever felt the need to **C**ut down on your drinking?
- Have you ever felt **A**nnoyed by criticism of your drinking?
- Have you ever felt **G**uilty about your drinking?
- Have you ever felt the need to drink a morning **E**ye-opener?

When two of the four questions are answered yes, it has 90% specificity in identifying problem drinking. The problems in CAGE are its lesser reliability in women and pregnancy.

The TWEAK questionnaire helps to identify at risk pregnant drinkers

Table 12. The TWEAK Questionnaire.

- Can you hold six or more drinks? (**T**olerance)
- Are your friends or relatives **W**orried about your drinking?
- Have you ever had an **E**ye-opener (morning drinking to get going)?
- Have you ever had blackouts (**A**mnesia)?
- Have you ever felt the need to "**K**ut" down on your drinking?

The Michigan Alcoholism Screening Test (MAST) is a 25 item questionnaire used to identify abuse. But it is cumbersome and could not be used easily.

Alcohol Use Disorders Identification Test (AUDIT) is a 10-item questionnaire designed by the WHO for screening of problem drinking . The first three questions are used to assess the quantity, frequency, and peak intensity of drinking and the next Seven questions deal with issues in the past year. The AUDIT is scored by means of summation of the weights associated with the response selected for each item.

A total $\geq$ 8 for men up to age 60, or $\geq$ 7 for women, adolescents, or men over age 60 is considered a positive screening test.. Any value greater than this suggests alcohol abuse; higher values increase the reliability of the diagnosis of alcohol abuse. The AUDIT score has been considered a better predictor of social problems than laboratory markers

AUDIT can be finished in 2 to 4 minutes. At the end of first question if the patient says no drinking in the previous year we can straightaway go to the ninth question. Likewise if the patient has a sum score of 0 on second and third question, we can straightaway go to the ninth question. In this way AUDIT can be shortened. The advantages of AUDIT are:

- It identifies drinkers who are at risk of dependency
- It quantitates the amount consumed
- It inculcates short-term as well as long-term drinking patterns
- Takes less time
- Can be done in an easier way
- Accuracy is more
- Easily computed and compared for epidemiological purposes

The ability to predict the existence of other alcohol-related illnesses on the basis of AUDIT results was similar to that with laboratory tests.

Laboratory tests are needed to confirm the diagnosis. Clinical differentiation of the stages of ALD is difficult at times, and no clinical sign definitively say that alcohol as the cause of liver disease.

The Alcohol Use Disorders Identification Test (AUDIT)		
1	How often do you have a drink containing alcohol?	Never / Monthly or less / 2-4 times a month / 2-3 times a week / 4 or more times a week
2	How many standard drinks containing alcohol do you have on a typical day when drinking?	1 or 2 / 3 or 4 / 5 or 6 / 7 to 9 / 10 or more
3	How often do you have six or more drinks on one occasion?	Never / Less than monthly / Monthly / Weekly / Daily or almost daily
4	During the past year, how often have you found that you were not able to stop drinking once you had started?	Never / Less than monthly / Monthly / Weekly / Daily or almost daily
5	During the past year, how often have you failed to do what was normally expected of you because of drinking?	Never / Less than monthly /Monthly / Weekly / Daily or almost daily
6	During the past year, how often have you needed a drink in the morning to get yourself going after a heavy drinking session?	Never / Less than monthly / Monthly / Weekly / Daily or almost daily
7	During the past year, how often have you had a feeling of guilt or remorse after drinking?	Never / Less than monthly / Monthly / Weekly / Daily or almost daily
8	During the past year, have you been unable to remember what happened the night before because you had been drinking?	Never / Less than monthly / Monthly / Weekly / Daily or almost daily
9	Have you or someone else been injured as a result of your drinking?	No / Yes, but not in the past year / Yes, during the past year
10	Has a relative or friend, doctor, or other health worker been concerned about your drinking or suggested you cut down?	No / Yes, but not in the past year / Yes, during the past year

Each question will be given points ranging from 0 to 4. A total ≥ 8 for men up to age 60, or ≥ 7 for women, adolescents, or men over age 60 is considered a positive screening test.

Management based on AUDIT :

AUDIT SCORE	Intervention
0-7	Health education
8-15	Advice
16-19	Advice + counselling + continuous monitoring
20-40	Referral to specialist

AUDIT has been designed to cover all the problems related to drinking:

- If a drinker has a score of ≥ 1 on 2^{nd} or 3^{rd} question, it implies hazardous consumption
- A score above 0 on questions 4 to 6 shows alcohol dependence
- Scores above 0 on 7^{th} to 10^{th} questions denotes that the patient is currently experiencing the problems related to alcoholism

Blood or breath alcohol measurements are the most sensitive and specific indicators of recent alcohol abuse, particularly for binge drinkers. The major limitation of these tests is the short half-life of ethanol in blood, urine, and breath.

Biomarkers of alcohol abuse that are detectable over longer periods can be used. The most specific of these biomarkers is carbohydrate-deficient transferrin (CDT). CDT levels increase in serum with ingestion of 50 to 80 g/day of ethanol for two to three weeks and decline gradually during abstinence, with a half-life of approximately 15 days. The problem with CDT is it has a sensitivity of only 35% to 40% if consumption is 100 g of ethanol daily. Also it is influenced by various factors like age, sex, body mass index, etc. Hence it is not used in clinical practice. It is a FDA approved test. Other parameters include MCV, GGTP levels and ratio of mitochondrial AST to total AST.

Alcoholic hepatitis:

Alcoholic hepatitis is a clinical syndrome of icterus and hepatic dysfunction that usually manifests following continuous excessive alcohol intake[average of 100 g /day]. The usual age at which the disease presents is 40 to 60 years, but can vary from 20 to 80 years. The cardinal sign is rapid onset of jaundice. Typically, the liver is enlarged and tender[6]. The importance of alcoholic hepatitis lies in its potential reversibility.

Documentation of chronic and significant alcohol abuse is important. Minimum of 80 g/day for 5 years is typical. Patient may have stopped alcohol consumption several weeks before, but Clinical presentation after 3 months of abstinence should raise doubts about the diagnosis of alcoholic hepatitis and these patients should be evaluated for other causes of liver damage such as cirrhosis and sepsis[8].

HISTOLOGY:

Ballooning:

The hepatocytes becomes swollen due to accumulation of fat, proteins and water. Later they become necrosed.

Mallory bodies:

Accumulation of intermediate filaments are seen as eosinophilic cytoplasmic inclusions. They are called Mallory bodies. they are non-specific.

They can be present in Wilsons disease, primary biliary cirrhosis, chronic Cholestasis and liver malignancy.

Neutrophil infiltration:

Neutrophils surround the degenerating hepatocytes. They have

predilection to involve hepatocytes with Mallory bodies. lymphocytes and macrophages are also recruited.

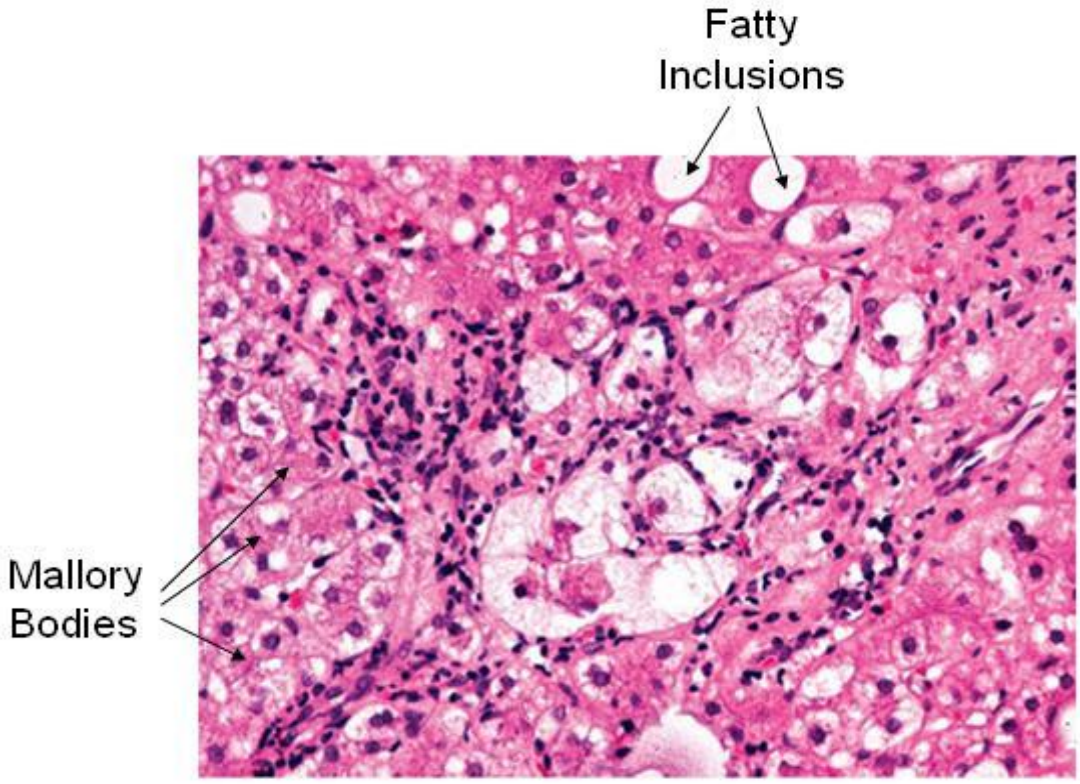
Fibrosis:

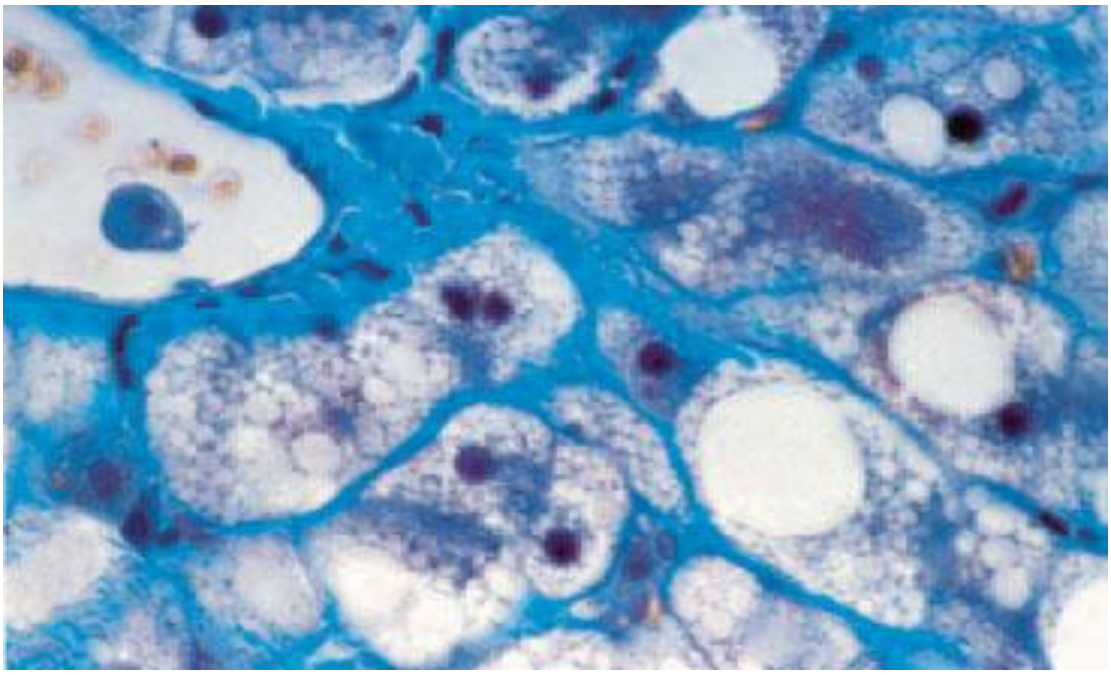
Sinusoidal and perivenular fibrosis occurs.it is predominantly found in zone 3. Periportal fibrosis will be the dominant picture in repeated bouts of heavy drinking.

Cholestasis :

Mortality is increased in marked cholestasis.

The histology varies depending on the severity of the disease. These histological changes can be seen in NASH too. Hence, in a patient with adequate alcohol intake history and laboratory features, histology is the gold standard for the diagnosis of alcoholic hepatitis





Picture showing ballooning of hepatocytes, micro and macrovesicular steatosis and Mallory hyalin

DIAGNOSIS IN CLINICAL PRACTICE:

However there are problems in clinical setting in obtaining biopsy. If the patient has ascites and/or coagulopathy, percutaneous liver biopsy cannot be performed. Still transjugular biopsy can be done, but this needs expertise which may not be immediately available. Even if biopsy is done, if it is relied upon for diagnosis, delay in management will occur.

Hence in practice, the disease is suspected when icterus and other symptoms and signs of decompensation like ascites happens to an individual with excess ethanol intake[4] . however in the study conducted by HISLOP et al in Scotland and north east England biopsy done in the patients showed that only 65% of biopsy proven disease had icterus and 5% had encephalopathy.

The common presentations in biopsy proven alcoholic hepatitis includes a wide range of signs and symptoms like vomiting, hepatomegaly, ascites, splenomegaly, encephalopathy, etc

Clinical diagnosis has an accuracy of about 80% when compared with histology. However, along with history of chronic excess alcohol ingestion,AST < 500 [or ALT < 300] and exclusion of autoimmune ,chronic viral or malignant diseases if serum bilirubin was set at a minimum level of > 80 µmol/l[4.67 mg/dl] the accuracy becomes 99.2%. in this study too the

inclusion criteria of serum bilirubin is > 5 mg/dl to improve the diagnostic accuracy.

Approximately 50-60 % patients will also have co-existing cirrhosis. But this doesnot seem to worsen the 28 day and 84 day mortality of patients. The reason for poor prognosis in these patients are pro-inflammatory Processes

CLINICAL FEATURES:

It can be divided into 4 types:

1] Features specific to existing alcoholic hepatitis- although clinical jaundice occurs only in 40-60% of cases , all cases will have hyperbilirubinemia. Other features include right upper quadrant pain, fever, tachycardia. Fever can be in the range of 100.4 to 104 F. This fever can be attributed to alcoholic hepatitis only after excluding infections and malignancy. Malnutrition can be present in upto 90% patients . severe disease can have hepatic encepahalopathy, renal failure,ascites.

2] Features due to underlying cirrhosis – this includes spider naevi, palmar erythema

3] Features of associated diseases – like co-existing infections

4] Features of alcohol withdrawal – the frequency of alcohol withdrawal is inversely proportional to the severity of the disease

Laboratory features:

Liver function tests:

Liver enzymes:

The usual picture will be an increase in AST and ALT to two-to seven fold. Usually the AST/ALT ratio usually is of little value in differentiating various hepatobiliary disorders. One of the exceptions to this is the recognition of alcoholic liver disease. If the ALT is less than 300 IU , an AST/ALT ratio more than 2 suggests alcoholic liver disease; a ratio greater than 3 is highly suggestive of alcoholic liver disease. The increased ratio shows the decresed ALT level in patients with alcoholic liver disease. This is secondary to a deficiency of pyridoxal 5′-phosphate . although both AST and ALT needs pyridoxal 5'-phosphate, the requirement of ALT is more. The altered AST/ALT ratio in serum appears to reflect the altered ratios in the liver.

Very high levels suggest complicating paracetamol ingestion. A Smaller dose of paracetamol can predispose alcoholics into severe hepatitis. Levels of more than 500 suggests causes other than alcoholic hepatitis.This is because of alcohol induced induction of CYP450 in MEOS[microsomal enzyme oxidising systems]. This increased MEOS activity causes increased production of toxic metabolite of paracetamol, N-acetyl-P-benzoquininemine[NAPQ]. A variant of alcoholic hepatitis called alcoholic foamy degeneration can cause AST to raise

upto 730 u/l. Despite striking elevations, the AST/ALT ratio remains increased and typical of alcoholic liver disease.

Serum ALP levels will be increased to modest amount of upto three times upper limit of normal. Regarding the clinical value of GGT, its use lies in conferring organ specificity to an elevated value of alkaline phosphatase, because GGT activity is not elevated in patients with bone disease. In addition, high GGT values are found in patients who take medications such as barbiturates or phenytoin or ingest large quantities of alcohol , even when other serum enzyme and bilirubin values are normal. When the elevated GGT value is associated with the use of anticonvulsant drugs or alcohol abuse, no correlation between serum GGT and alkaline phosphatase values is seen. Aside from its value in conferring liver specificity to an elevated alkaline phosphatase

level and its possible use in identifying that a patient abuses alcohol, GGT testing offers no advantage over aminotransferase and alkaline phosphatase testing.

Serum albumin:

The long serum half-life of albumin in serum accounts for its unreliability as a marker of hepatic synthetic function in acute liver injury. Serum albumin levels less than 3 g/dL in a patient with newly diagnosed hepatitis should raise

suspicion of a chronic process . Serum albumin is an excellent marker of hepatic synthetic function in patients with chronic liver disease and cirrhosis, with the exception of patients with cirrhosis and ascites, who may have normal or increased albumin production but an increased volume of distribution that results in a low serum albumin level.

When it is less than 2.5 mg/dl , it indicates severe disease. Serially increasing albumin levels shows that the patient is improving. Because of its low prognostic value in acute hepatic diseases it is not used in the prognostic scoring in alcoholic hepatitis

Serum bilirubin:

In other diseases total serum bilirubin level is not a sensitive indicator of hepatic dysfunction and may not accurately reflect the degree of liver damage. Hyperbilirubinemia may not be detected in instances of moderate to severe hepatic parenchymal damage or a partially or briefly obstructed common bile duct. Few controlled studies have critically assessed the prognostic value of magnitude and duration of hyperbilirubinemia in liver disease and have shown that In acute alcoholic hepatitis, hyperbilirubinemia correlates with a poor prognosis. Levels > 8 mg/dl indicates severe disease.

Also in severe disease, it is measured 1 week after starting steroids to determine the response to treatment.

PT/INR:

Measurement of the prothrombin time in patients with liver disease is most useful in cases of acute liver disease. Unlike the serum albumin, the prothrombin time allows an assessment of current hepatic synthetic function; factor VII has the shortest serum half-life (six hours) of all the clotting factors. It also correlates with severity of disease. The prothrombin test is not a sensitive index of chronic liver disease because, even in severe cirrhosis, prothrombin levels can be normal or the prothrombin time prolonged only slightly.

Also it has high prognostic value, particularly for patients with acute hepatocellular disease. An abnormal prothrombin time with confirmed prolongation more than 5 to 6 seconds above control often precedes by days the manifestations of liver failure. Progressive return of the prothrombin time to normal usually precedes or accompanies other evidence of clinical improvement. The degree of prolongation of the prothrombin time is a prognostic factor for patients with alcoholic steatonecrosis. A prothrombin time greater than 4 seconds above control value occurred six times as often in a group of patients who died (60%) than in a group who survived (10%).

Complete Blood Count:

It shows mild anemia(usually macrocytic), platelets in the range of normal to decreased and elevated white cell count. White cell count elevation to upto 40,000 are common. PMN > 5500 in the presence of m DF > 32 indicates poor prognosis. The presence of leukemoid reaction implies very poor prognosis. Since patients present with fever and leukocytosis clinicians will always have a concern for sepsis alcoholics , being malnourished are at increased risk of infection. Hence a minimum evaluation for fever should include chest x ray, blood culture, paracentesis(if ascites is present), urine analysis and culture and specific testing if localised signs of infection are present. After ruling out infection, the fever can be attributed to alcoholic hepatitis.

RENAL FUNCTION TESTS

The values of urea and creatinine rises. The patient can develop hepatorenal syndrome. Hepatorenal syndrome development is associated with 1 month mortality of 75%. These elevations are found to have statistically significant correlation with the severity of the disease. Hence the rise of urea and creatinine tells about the Prognosis.

ROLE OF LIVER BIOPSY:

Liver biopsy is useful but not necessary for the diagnosis. It assumes greater importance in the evaluation of patients who continue to have abnormal results of liver tests after a period of abstinence of approximately 3 to 4 months. It is difficult to identify the prothrombin time at which needle biopsy of the liver are contraindicated because the risk of bleeding has not been well correlated with the values of this test. The accepted cut-off value is PT prolongation of more than 4 seconds and INR>1.5.

ROLE OF IMAGING:

- The primary utility lies in identifying mass lesions like hepatocellular carcinoma and analysing the presence of cirrhosis
- It helps to rule out other diseases which might cause similar biochemical profile.
- If biopsy is planned, baseline imaging is done to evaluate silent mass lesions and to understand the anatomy
- MRI features which indicates ALD are caudate lobe enlargement and decreased regeneration
- However these differences are never absolute
- Also sonogram or CT cannot clearly delineate fatty liver from steatohepatitis.

Other investigations :

In the evaluation of patients with symptoms, nonspecific findings include elevated urate, lactate, and TGL levels and a decrease in magnesium, phosphate, and potassium levels. Polyclonal hyperglobulinemia and an increase in the circulating level of immunoglobulin A (IgA) also occurs with ALD It must be reiterated that no specific laboratory test exists that is specific for ALD.

A recently described tool for the diagnosis of ALD is hepatic phosphorus 31 magnetic resonance spectroscopy . This study is used to calculate hepatic energy metabolism and phospholipid membrane metabolism Lower phosphodiesterase to adenosine triphosphate ratios have been reported in patients with alcoholic cirrhosis

Frequent measurement of serum ethanol levels during office visits Can be done easily. But this is often-ignored method of assessing for alcohol use. Other laboratory parameters include β hexosaminidase and urinary 5 hydroxy tryptophol levels , which must be subjected to prospective testing at several centers before the validity can be confirmed.

Endoscopy:

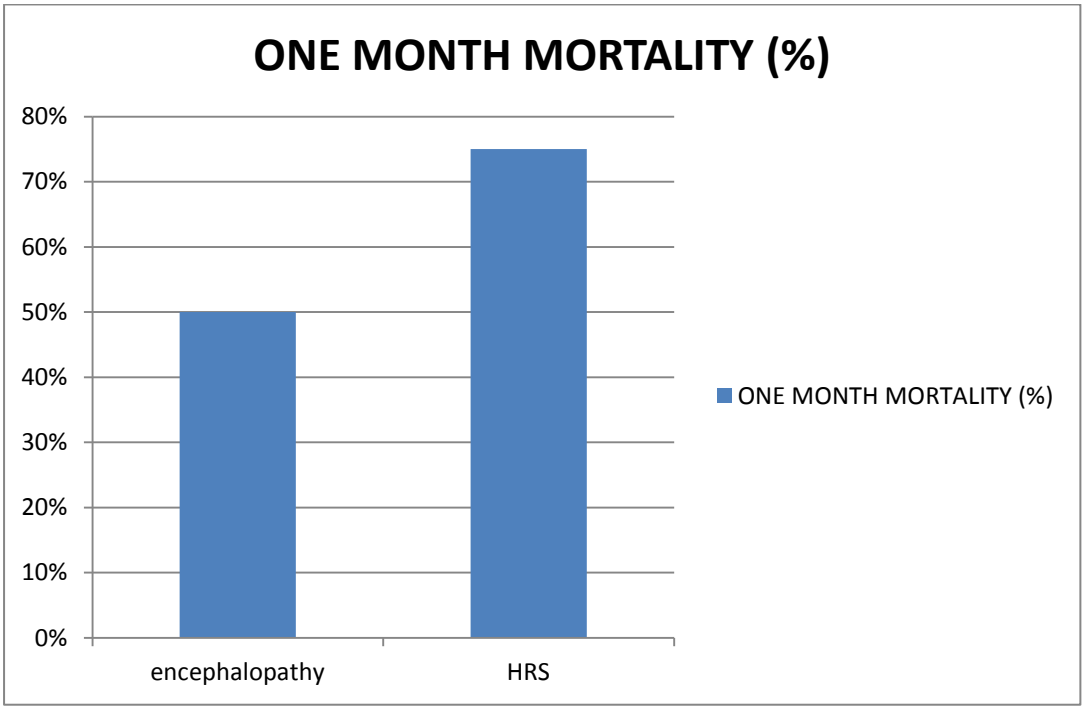
It is used when an alcoholic presents with active upper gastrointestinal bleeding. In the clinical situation of alcohol abuse, upper gastrointestinal

bleeding may be secondary to a variety of causes that include Mallory-Weiss tear, peptic ulcer disease, direct alcohol-induced gastric mucosal erosions and injury, portal hypertensive bleeding from varices, and congestive gastropathy secondary to cirrhosis. Alcohol abuse also is associated with a direct inhibitory effect on hepatic protein synthesis and a decrease in procoagulant factors that aggravate the bleeding once it begins. Therefore, endoscopy has both diagnostic and therapeutic value in such scenario.

PROGNOSIS :

The prognosis among patients with alcoholic hepatitis can vary dramatically. In patients with severe disease, the mortality rate is high, similar to that of acute fulminant hepatic failure. Severity can be identified by the occurrence of encephalopathy, significantly prolonged PT, very high serum

bilirubin level , depression of the serum albumin level, high serum creatinine level, and older age.



Three models have been shown to analyse short-term prognosis

1. mDF :

It is discovered by Maddrey and Boitnott. It is calculated as 4.6 × PT prolongation(Patient's− control value (seconds) + serum bilirubin (mg/dL). The mDF has proved useful for delineating 28 day and 84 day mortality. Evidence has proven that patients with a mDF value of 32 or more experience a worse prognosis, with 28 day mortality rates of 35% to 45%.

By contrast, patients with a mDF value less than 32 have short-term survival rates of 90% to 100%.

The MELD score (which includes the serum bilirubin level, INR along with creatinine level) and the Glasgow alcoholic hepatitis score (which includes age, WBC count, urea level, prothrombin time ratio [ratio of the patient's prothrombin time to the control value] along with serum bilirubin level) also have been shown to predict survival in patients with severe alcoholic hepatitis. Because both the MELD and Glasgow scores include measures of renal function, they appear to be more accurate than the mDF in determining the prognosis of patients.

Scoring Systems:

Discriminant Function = (4·6 x PT) +Serum Bilirubin (mg/dl)

Modified Discriminant Function = 4·6 X (PTPATIENT – PTCONTROL) + Serum Bilirubin (mg/dl)

Prognosis poor if score ≥ 32

MELD score = 3.78[Ln serum bilirubin (mg/dL)] + 11.2[Ln INR] + 9.57[Ln serum creatinine (mg/dL)] + 6.43

Prognosis poor if score ≥18

Glasgow Alcoholic Hepatitis Score

Score	1	2	3
AGE	<50	>50	
WCC(10^9)	<15	>15	
UREA(MMOL/L)	< 5	>5	
PT ratio or INR	<1.5	1.5 – 2	>2.0
Bilirubin(µmol/l)	<125	125-250	>250

Prognosis poor if score ≥ 9

The disadvantage in MELD score is that

1) It needs calculators for calculation since it involves logarithms

2) It includes creatinine as a measure of renal function. Evaluation of creatinine is commonly done based on jaffe reaction. In diseases associated with hyperbilirubinemia, creatinine will be underestimated.

   So the observed value based on jaffe's method needs correction, which is more cumbersome

GAHS is more easy to calculate and it uses urea as a measure of renal function

ABIC score :

(age x 0.1) + (serum bilirubin x 0.08) + (serum creatinine x 0.3) + (INR x 0.8)

Score ≥ 9 indicates poor prognosis

Lille score :

It is used to identify patients who donot respond to corticosteroids at the end of one week, so that alternate therapies can be considered. It combines 6 variables:

1.age

2. renal insufficiency

3. Albumin

4. prothrombin time

5. bilirubin, and

6. evolution of bilirubin at day 7.

All these variables have been studied and found that each is individually associated with altering the prognosis. A score > 0.45 signifies steroid failure and steroids should be stopped. These patients have a survival of 25 %.

The disadvantage is that it necessitates the need of calculators to calculate

MATERIALS AND METHODS

MATERIALS AND METHODS

STUDY DESIGN	:	OBSERVATIONAL STUDY
STUDY PLACE	:	Department of general medicine and medical gastroenterology Government Stanley Hospital, Chennai -1.
STUDY PERIOD	:	6 months (march 2012 – august 2012)
STUDY POPULATION	:	Patients admitted with alcoholic hepatitis
SAMPLE SIZE	:	50 patients
SAMPLING	:	Simple random sampling

Inclusion criteria:

- Pt. with hepatitis with alcohol consumption of > 80 g/day for 10 years.
- Bilirubin > 80 micromol/l
- AST < 500 u/l

Exclusion criteria:

- Alcohol intake < 20 g/day
- Pt. on amiodarone
- Hbs Ag positive
- Anti-HCV positive
- GI bleeders
- Autoimmune liver diseases
- Liver malignancy
- Inpatient stay of less than 48 hours

After getting approval from the institutional ethical committee, the study was started. All the individuals in this study were given information form and consent form. After signing the informed consent form they were enrolled in this study.

HOW THE STUDY WAS CONDUCTED

Patients admitted with alcoholic hepatitis were included in the study after applying the inclusion and exclusion criteria. They were subjected to thorough history , clinical examination , biochemical investigations, ultrasonogram of the abdomen. They were followed up after one month of their present admission.

Assessment panel includes-

- History , with specific focus on alcohol intake- amount, type and duration and with AUDIT score ≥ 8 in males and ≥ 7 in females and elderly males
- Age
- Biochemical investigations :
    - white cell count
    - serum urea
    - serum bilirubin

- PT and INR

- SGOT and SGPT

- Ultrasonogram of abdomen done to exclude cirrhosis and malignancy Results were duely collected and analysed

The patients were followed up for one month and the mortality is assessed mDF and GAHS were calculated. Downloadable calculators were used for calculation. These calculators requires only variables to be submitted.

Modified Discriminant Function :

4·6 (PTPATIENT – PTCONTROL) +Serum Bilirubin (mg/dl)

Glasgow Alcoholic Hepatitis Score

Score	1	2	3
AGE	<50	>50	
WCC(10^9)	<15	>15	
UREA(MMOL/L)	< 5	>5	
PT ratio or INR	<1.5	1.5 – 2	>2.0
Bilirubin(µmol/l)	<125	125-250	>250

The patients with m DF ≥ 32 were given prednisolone for four weeks and then tapered over next four weeks. If the patient had contraindications to steroids, pentoxifylline is given. The patients were followed for one month and the mortality is observed.

Sensitivity, specificity and accuracy of mDF and GAHS in calculating 1 month mortality were calculated. The results were analysed. P-value of 0.05 is considered statistically significant.

RESULTS

RESULTS

This study included 50 patients diagnosed with alcoholic hepatitis admitted in department of general medicine and medical gastroenterology, government Stanley hospital. The one month mortality prediction by modified discriminant function and GAHS score is calculated and compared with observed one month mortality. The results were tabulated and analysed as follows:

Table 1 . AGE DISTRIBUTION

AGE GROUP [years]	Number	Percentage
21-30	7	14
31-40	18	36
41-50	16	32
Above 51	9	18

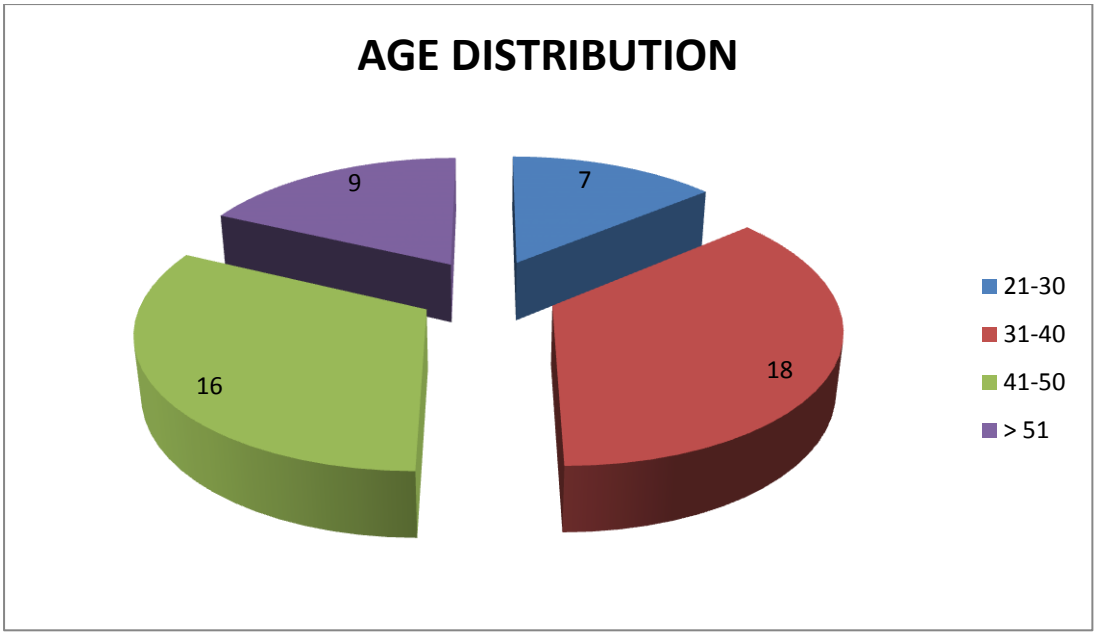
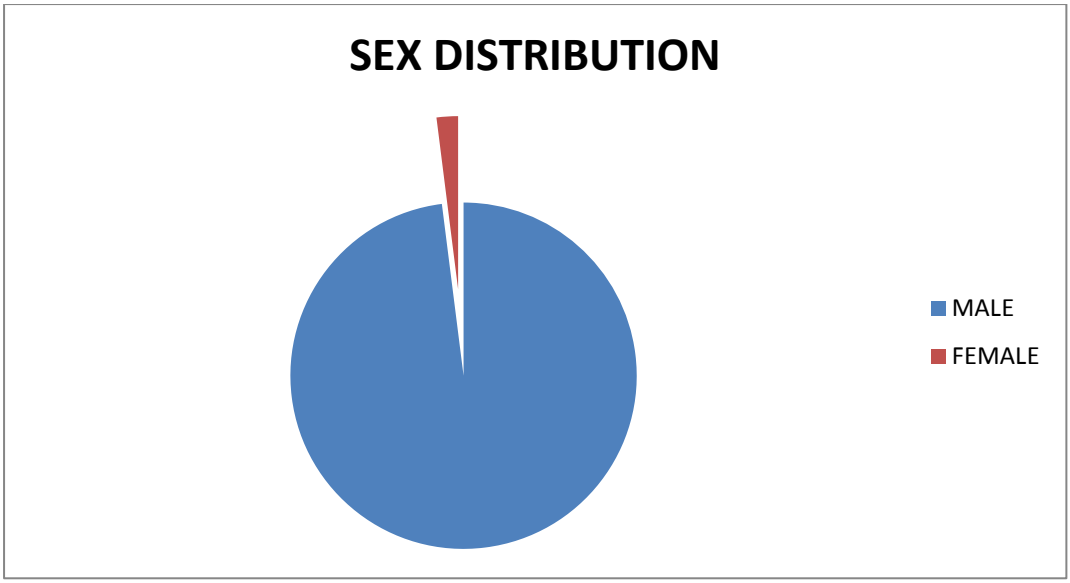


Table 2. Sex Distribution

SEX	NUMBER
Male	49
Female	1

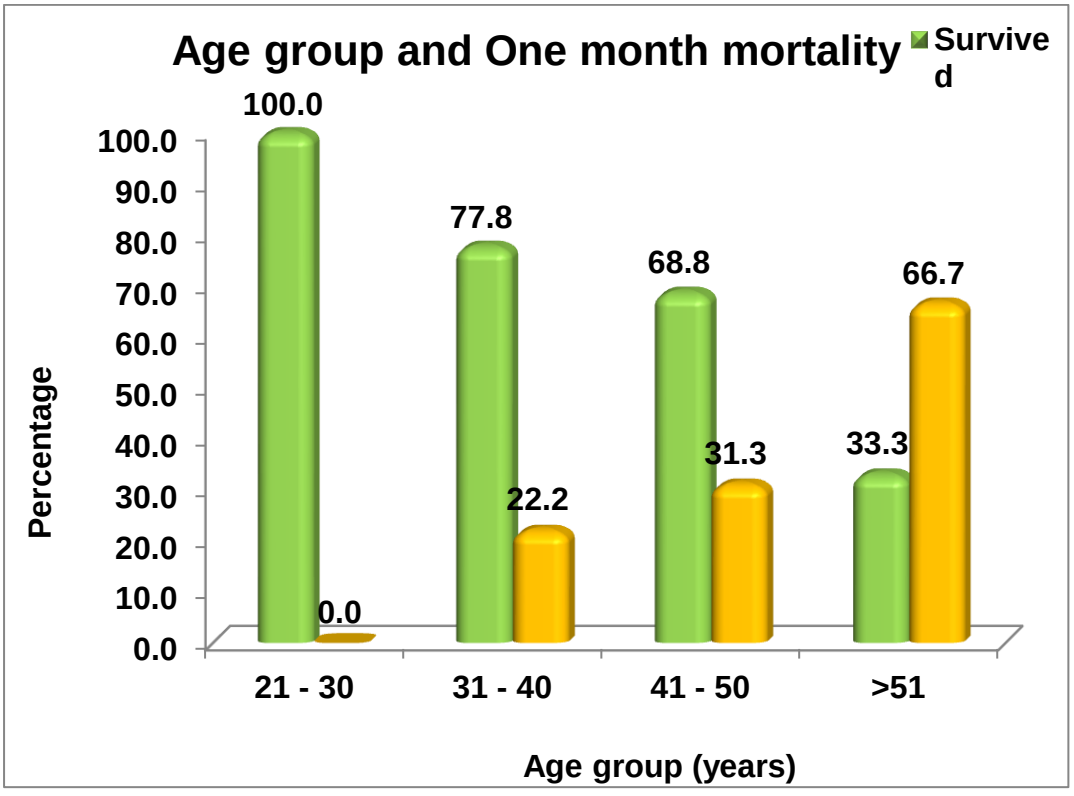


Majority in our study group are males

Trend Chi-square to compare the proportions

Age group (years)	1 month Mortality				Total		P-Value
	Survived		Died				
	N	%	N	%	N	%	
21 - 30	7	100.0	0	0.0	7	100.0	
31 - 40	14	77.8	4	22.2	18	100.0	
41 - 50	11	68.8	5	31.3	16	100.0	0.005
>51	3	33.3	6	66.7	9	100.0	
Total	35	70.0	15	30.0	50	100.0	

This table shows that as age increases, the mortality increases too.

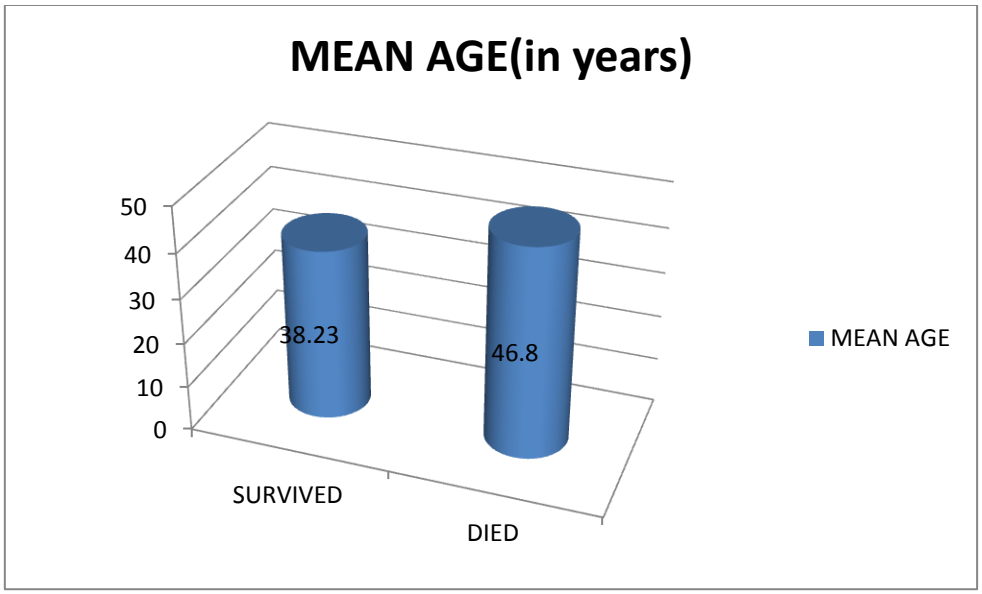


Independent samples t-Test to compare mean values between Variables

AGE

Variable	1 month Mortality	N	Mean	Std. Deviation	P-Value
Age (years)	Survived	35	38.23	7.99	0.002
	Died	15	46.80	9.33	

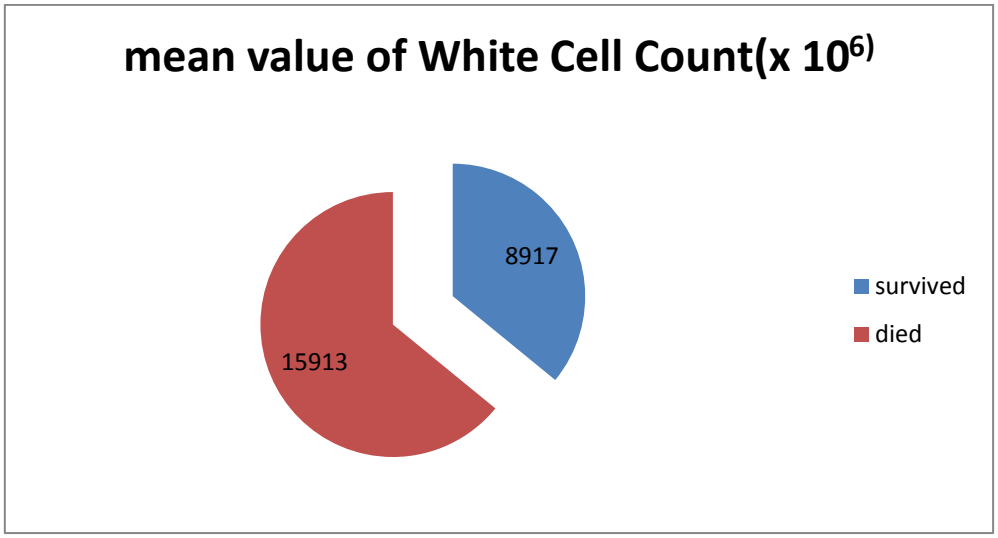
This table shows that patients who survived had a mean age of 38.23 whereas patients who died at the end of 1 month had a mean age of 46.8. This difference is significant as suggested by a p-value of 0.002



WHITE CELL COUNT

Variable	1 month Mortality	N	Mean	Std. Deviation	P-Value
WCC	Survived	35	8917.1	3324.5	<0.001
	Died	15	15913.3	4652.6	

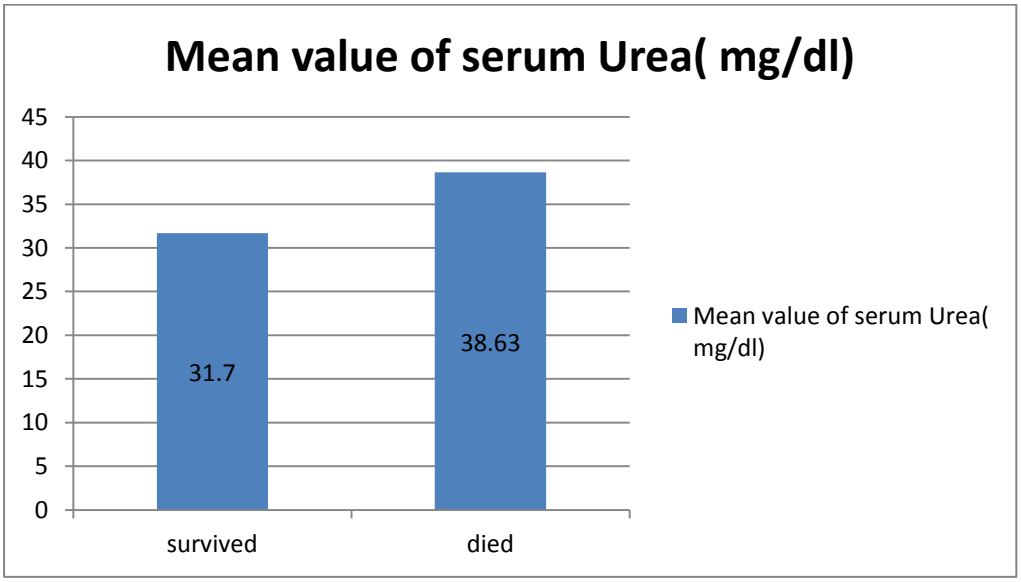
Patients who died at the end of 1 month had significantly raised white cell count(mean of 15913) with a p-value of < 0.001 indicating the importance of white cell count in indicating the prognosis of alcoholic hepatitis.



SERUM UREA

Variable	1 month Mortality	N	Mean	Std. Deviation	P-Value
Urea	Survived	35	31.74	8.98	0.014
	Died	15	38.63	8.15	

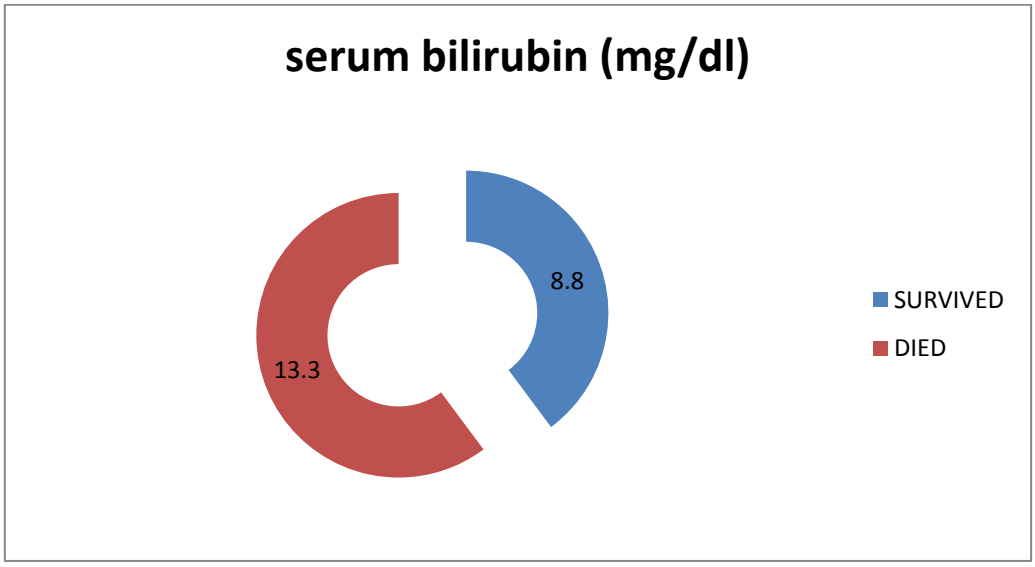
Patients who died at the end of 1 month had significant rise in urea compared to those survived(p- 0.014), indicating renal involvement altering the prognosis of alcoholic hepatitis



SERUM BILIRUBIN

Variable	1 month Mortality	N	Mean	Std. Deviation	P-Value
Total bilirubin	Survived	35	8.81	2.46	0.007
	Died	15	13.39	5.57	

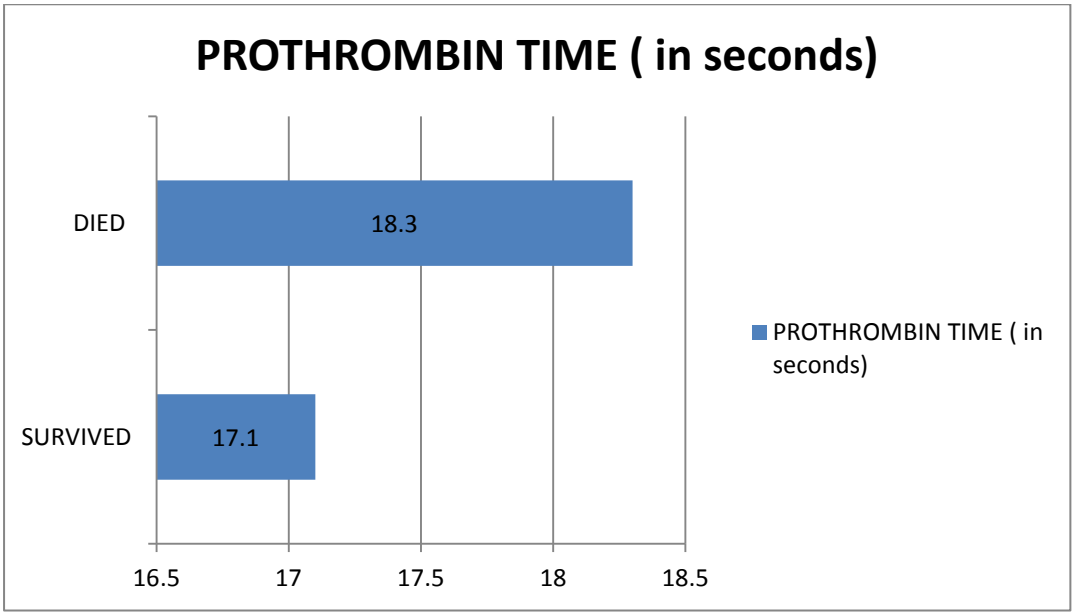
The average value of serum bilirubin in patients who died was 13.3,compared the value of 8.81 in those who survived (p- value = 0.007) indicating it's value in assessing the prognosis



PROTHROMBIN TIME:

Variable	1 month Mortality	N	Mean	Std. Deviation	P-Value
PT	Survived	35	17.17	2.07	0.073
	Died	15	18.33	2.02	

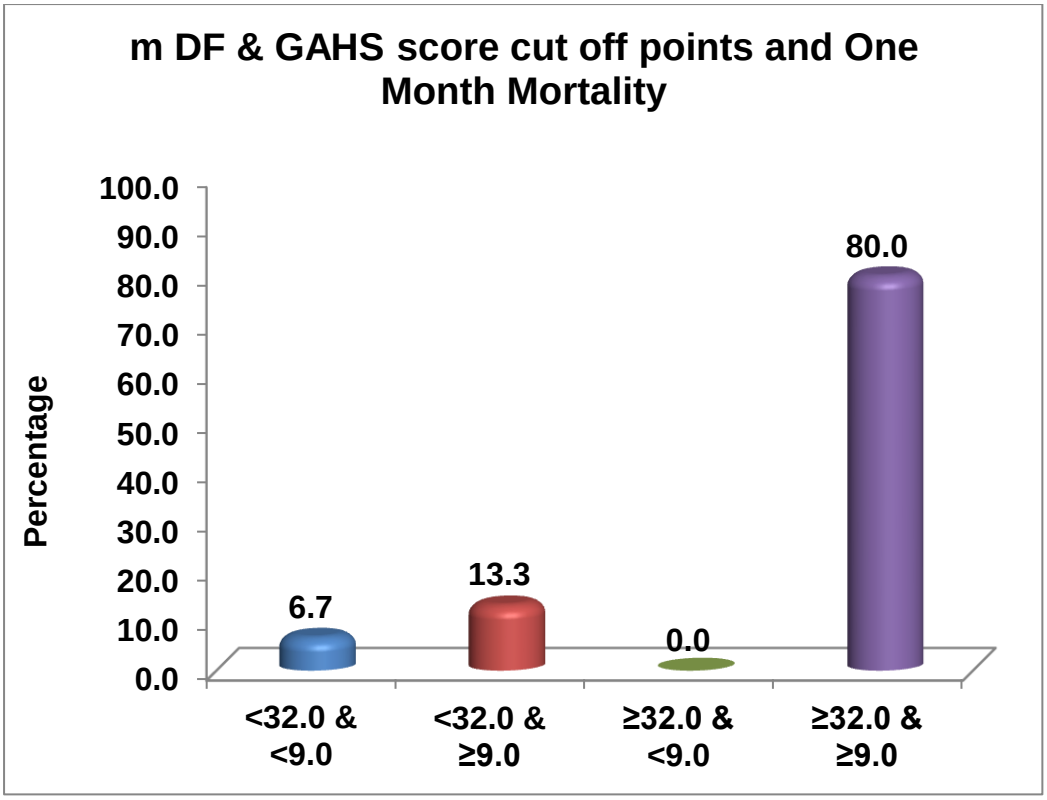
In our study, the prothrombin time among the patients who died was raised Compared to those who survived, but this rise was not statistically significant(p- value - 0.073).



Comparison of mDF and GAHS in patients who died at 1 month :

m DF and GAHS score	Died	
	N	%
m DF<32.0 & GAHS<9.0	1	6.7
m DF<32.0 & GAHS≥9.0	2	13.3
m DF≥32.0 & GAHS<9.0	0	0.0
m DF≥32.0 & GAHS≥9.0	12	80.0
Total	15	100.0

Of the 15 patients who died , 12 were detected as having severe disease by both mDF and GAHS. But 2 patients who had mDF < 32 and GAHS ≥9 died. These patients if identified as severe , could have benefitted with steroids or pentoxifylline. 1 patient who had both mDF < 32 and GAHS < 9 died and both scores failed to identify the severity. GAHS identifies severity in all patients identified by mDF ≥ 32, apart from identifying severe disease in patients with mDF < 32. The only patient where GAHS failed, mDF too failed to identify the severity .


m DF & GAHS score cut off points and One Month Mortality
Percentage
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
6.7
13.3
0.0
80.0
<32.0 & <9.0
<32.0 & ≥9.0
≥32.0 & <9.0
≥32.0 & ≥9.0

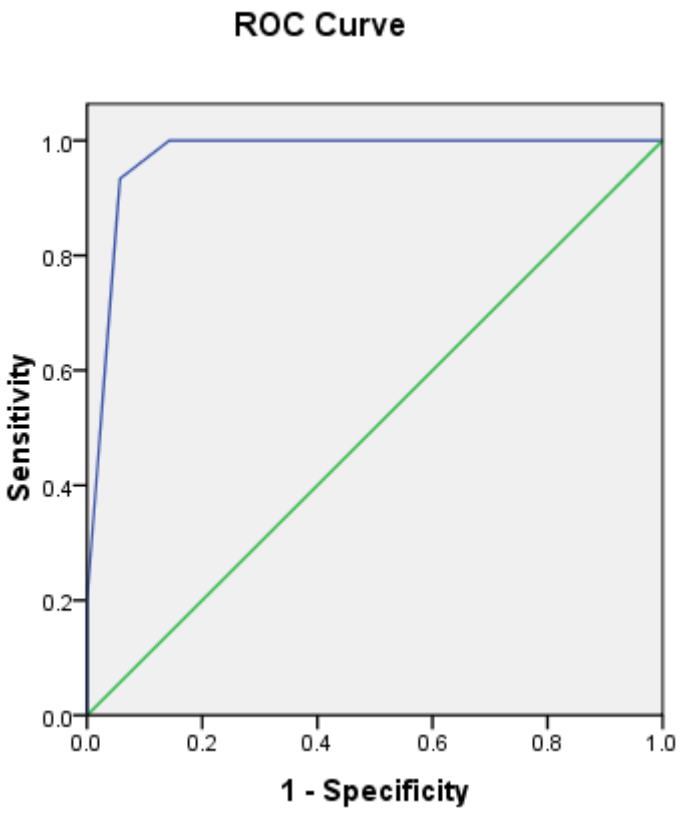
Kappa Statistics to measure the Agreement between the two scoring procedures

		m DF Score		Total
		≥ 32.0	< 32.0	
GAHS Score	≥ 9	14	2	16
	< 9	9	25	34
Total		23	27	50

Measure of Agreement	Value	P-Value.
Kappa	0.547	<0.001

Kappa value of 0.547 shows moderate agreement between GAHS and mDF .

ROC Curve analysis to find out the best cut off point for GAHS to predict the 1 month mortality.



Area Under the Curve = 0.972

The ROC curve analysis suggests that GAHS value ≥ 9.0 is the best cut-off point to predict the 1 month mortality.

Sensitivity Specificity Analysis for mDF

		1 month Mortality		Total
		Died	Survived	
m DF Score	≥ 32	13	12	25
	< 32	2	23	25
Total		15	35	50

Parameter	**Estimate (%)**	**Lower - Upper 95% CIs**
Sensitivity	86.67	62.12, 96.26
Specificity	65.71	49.15, 79.17
Positive Predictive Value	52.00	33.50, 69.97
Negative Predictive Value	92.00	75.03, 97.78
Diagnostic Accuracy	72.00	58.33, 82.53

Thus mDF has a accuracy of 72 % in predicting 1 month mortality. Also, out of 25 patients who had discriminant function of > 32, 13 patients died and 12 survived with a specificity of 65.7 %. Out of 25 patients who had score < 32 , 2 patients died. Also , the positive predictive value is low(52%)

Sensitivity Specificity Analysis for GAHS :

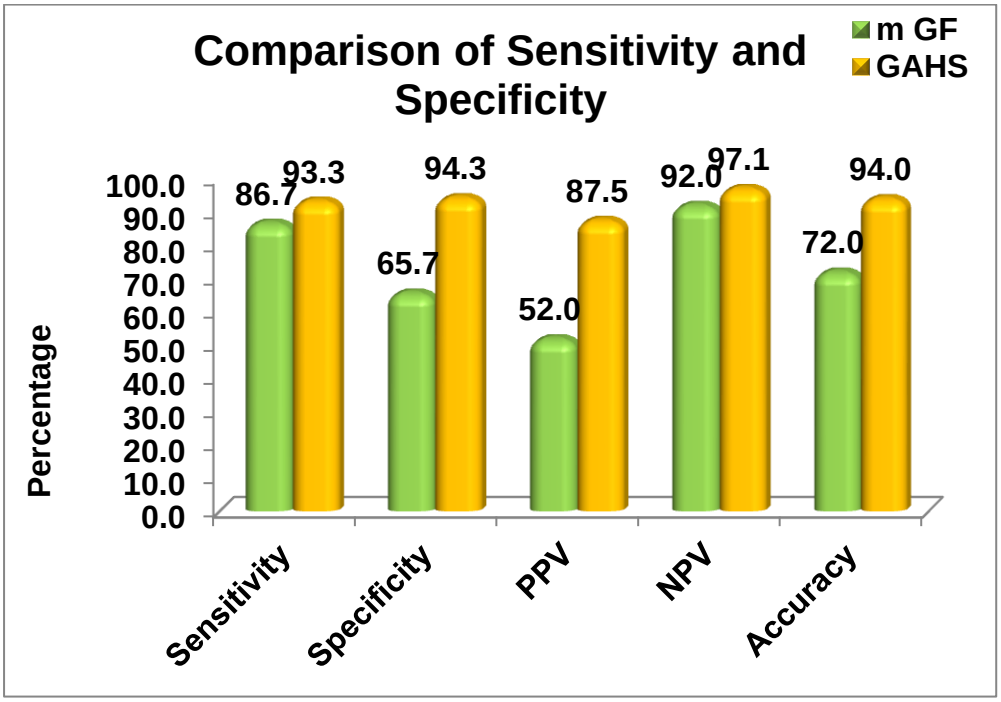
		1 month Mortality		Total
		Died	Survived	
GAHS Score	≥ 9	14	2	16
	< 9	1	33	34
Total		15	35	50

Parameter	**Estimate (%)**	**Lower - Upper 95% CIs**
Sensitivity	93.33	70.18, 98.81
Specificity	94.29	81.39, 98.42
Positive Predictive Value	87.50	63.98, 96.50
Negative Predictive Value	97.06	85.08, 99.48
Diagnostic Accuracy	94.00	83.78, 97.94

Thus GAHS has higher sensitivity,specificity, Positive predictive value, negative predictive value and diagnostic accuracy when compared to mDF .

Among these, the SPECIFICITY, POSITIVE PREDICTIVE VALUE and ACCURACY of GAHS is SIGNIFICANTLY HIGHER compared to mDF . Hence GAHS identifies the severity of alcoholic hepatitis accurately compared to mDF and this should be used in deciding upon treatment with steroids or pentoxifylline.

Parameter	**mDF**	**GAHS**
Sensitivity	86.67	93.33
Specificity	65.71	94.29
Positive Predictive Value	52.00	87.50
Negative Predictive Value	92.00	97.06
Diagnostic Accuracy	72.00	94.00



DISCUSSION

DISCUSSION

Alcoholic hepatitis is one of the most prevalent disease. It is increasing day by day because of widespread use of alcohol. When severe, the short term mortality is very high. This high mortality is mainly due to inflammatory processes occurring in acute alcoholic hepatitis.

Identification of patients with severe disease is of key significance because these patients can be treated with steroids or pentoxifylline and these patients need to be monitored for the development of complications like hepatic encephalopathy and renal failure. Also these patients need to be followed up periodically because alcoholic hepatitis, in the long run is associated with nine times increased risk of development of cirrhosis.

The severity of disease is identified by mDF score ≥ 32. But the problem with this score is that it involves only serum bilirubin and Prothrombin time. It doesnot include any markers for inflammation or renal involvement.

The MELD score is cumbersome to calculate and it too doesnot involve any marker for inflammation. The GAHS is easy to calculate, involves markers for renal involvement and inflammation and is much more accurate than mDF .

Our study which was an observational study involved 50 patients with alcoholic hepatitis and comparison of actual prognosis with prognosis and severity calculated by mDF and GAHS.

The observed mortality was 30% . The severity predicted by GAHS had an accuracy of 94 % compared to that calculated by mDF which had 72% accuracy. Thus it is obvious that GAHS has much better severity prediction compared to mDF and this is helpful in treating patients. Also patients with GAHS < 9 survived, irrespective of their mDF, even if mDF ≥ 32. This shows that if GAHS < 9 , these patients need not be treated with steroids or pentoxifylline.

There are many studies reported in literature, comparing the various prognostic scoring systems. In the E H Forrest et al study, 241 patients were studied. The day of admission GAHS was statistically significant than mDF in finding out 28 and 84 day mortality. When compared with MELD , the day 1 GAHS was equally accurate in predicting 28 day mortality and more accurate in predicting day 84 outcome.

In the study conducted by Altamirano-Gomez J et al in mexico, 120 patients were studied. It was found that in-hospital mortality prediction of GAHS and MELD were superior compared to mDF and the prediction of in-hospital survival after fitting best cut-off points were similar.

In the study conducted by Sandahl TD et al in Denmark in 274 patients, the predicted 28-, 84- and 180 –day mortality of the patients by GAHS, MELD and ABIC scores were found to be similar. Rescoring on day seven improved the models predictions.

In the study conducted by H. Lafferty et al, 182 patients were assessed prospectively and compared with historical group which was treated as per mDF. At GAHS < 9, the survival rate at day 28 and day 84 were similar. If admission GAHS ≥ 9 who were treated had survival of 71 % at day 28, compared to 41 % of the comparison group with a p-value of 0.0002. at day 84, the survival rate was 54 % in the study group and 37 % in the historical group with a p-value of 0.008. this shows significant improvement in the outcome in patients treated as per GAHS grading of severity.

In the study by AJ Morris et al, 225 patients with mDF ≥ 32 ere studied. It was found that even if mDF ≥ 32, if GAHS < 9, there was no significant benefit in treating these patients with steroids. And patients with GAHS ≥ 9 had a very high mortality if corticosteroids are not given or they are contraindicated.

In N Palaniappan's work done at Nottingham, 44 patients with biopsy proven alcoholic hepatitis were studied. It was found out that mDF, MELD , GAHS and ABIC scores were similar in accuracy in predicting short-term mortality. All these scoring systems were poor in predicting long-term mortality. The CP score is found to be a poor predictor of both short and long term mortality.

S Ali studied 82 patients in UK and found that mDF , CP and GAHS were of equal accuracy in predicting 28 day mortality. In addition , very high PT, raised creatinine, gastro-intestinal bleeding and encephalopathy at the time of admission are associated with increased mortality.

studies	Population (number)	Results
EH Forrest	241	GAHS more accurate than mDF in predicting 28 and 84 day mortality
Altamirano- Gomez	120	GAHS superior to mDF in predicting in-hospital mortality
Sandahl	274	GAHS, MELD and ABIC scores are equal in accuracy
H Lafferty	182	Improvement in outcome if patients are treated with GAHS grading for severity.
AJ Morris	225	At GAHS < 9, no significant benefits with coticosteroids. ≥ 9 has poor prognosis if not treated
N Palaniappan	44	mDF , MELD,GAHS and ABIC are equal in accuracy. CP score is poor in accuracy.
S . Ali	82	mDF , CP, GAHS are equal in accuracy.

These studies show the accuracy of GAHS in comparison with other prognostic scoring systems.

Winding up, in our study of 50 patients

1] the GAHS score(94 %) accurately predicted 1 month mortality when compared with mDF (72 %) .

2] The specificity and positive predictive value of GAHS (94.3% and 87.5%) were far more superior compared to mDF (65.7 % and 52 %)

3] Out of the 25 patients with mDF < 32, three patients died. Of these three patients, two had GAHS ≥ 9 indicating that had GAHS been used to identify the severity, these patients could have benefitted with treatment of corticosteroids or pentoxifylline.

4] One patient who died had both GAHS < 9 and mDF <32. In this case, both scores failed to identify the severity

5] Each factor included in GAHS – age, bilirubin, urea and White cell count, with exception of prothrombin time had statistically significant rise in those patients who died compared to the survivors, indicating that each factor itself gives a clue to the prognosis of the disease.

LIMITATIONS OF THE STUDY:

1. Very small sample size.

2. Study group has predominantly males.

3. Liver biopsy was not done.

4. Africans and Americans were not included in the study

5. The source of error could possibly due to intra-individual variability in the laboratory measurement of white cell count, bilirubin, urea and PT.

SUMMARY
AND
CONCLUSIONS

SUMMARY AND CONCLUSIONS

1] Both mDF and GAHS predicts one month mortality in alcoholic hepatitis

2] GAHS has higher accuracy compared mDF . out of three patients with severe disease which mDF failed to identify, two were identified by GAHS

3] GAHS is easy to calculate.

4] Both mDF and GAHS failed to identify severe disease in one patient . This could be due to

- Lack of standardisation in measuring laboratory parameters.
- Small sample size
- Lacunae in the scoring systems

- Africans and Americans not included in the study

Extensive research work are under process, which may bring out accurate, easily calculable prognostic scoring systems which could identify patients with severe disease, so that the high short-term mortality associated with severe alcoholic hepatitis can be easily identified and treated and unnecessary corticosteroid therapy can be avoided. Alcoholic hepatitis being a potentially reversible condition , the high short-term mortality of 40-50 % is unacceptable and it has to be prevented. Let us hope we will achieve this in the near future.

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INSTITUTIONAL ETHICAL COMMITTEE
STANLEY MEDICAL COLLEGE, CHENNAI-1

Title of the Work	:	Comparison of modified Discriminant function and Glasgow Alcoholic Hepatitis score in alcoholic hepatitis in Predicting 1 month mortality.
Principal Investigator	:	Dr. G. Rengaraj
Designation	:	PG in M.D (Gen. Med.)
Department	:	Department of General Medicine Government Stanley Medical College, Chennai - 1.

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 06.03.2012 at the Council Hall, Stanley Medical College, Chennai - 1 at 2 PM

The members of the Committee, the secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

1. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
2. You should not deviate from the area of the work for which you applied for ethical clearance.
3. You should inform the IEC immediately, in case of any adverse events or serious adverse reaction.
4. You should abide to the rules and regulation of the institution(s).
5. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
6. You should submit the summary of the work to the ethical committee on completion of the work.

MEMBER SECRETARY,
IEC, SMC, CHENNAI.

சுய ஒப்புதல் படிவம்

ஆய்வு செய்யப்படும் தலைப்பு

"சாராய கல்லீரல் அழற்சி நோய் (Alcoholic Hepatitis) உள்ளவர்களில் எம்.டி.எஃப் (டிஸ்கிரிமினன்ட் ஃபங்ஷன்) மற்றும் க்ளாஸ்கோ ஸ்கோர் இடையே ஒப்பிட்டுப் பார்க்கும் ஓர் ஆய்வு"

ஆராய்ச்சி நிலையம் : அரசு ஸ்டான்லி மருத்துவமனை
சென்னை - 600 001.

பங்கு பெறும் நோயாளியின் பெயர் : வயது :

பங்கு பெறும் நோயாளியின் எண் : பாலினம் : ஆண் ☐ பெண் ☐

நோயாளியின் விலாசம் :

நோயாளி இதனை (✓) குறிக்கவும்.

மேலே குறிப்பிடப்பட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும். அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டது. ☐

நான் என்னை இவ்வாய்வில் தன்னிச்சையாகதான் பங்கேற்க அனுமதிக்கிறேன். எந்த காரணத்தினாலோ எந்த கட்டத்திலும் எந்த சட்ட சிக்கலுக்கும் உட்படாமல் என்னை இவ்வாய்வில் இருந்து விலக்கி கொள்ளலாம் என்றும் அறிந்து கொண்டேன். ☐

இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்த மேலும் ஆய்வு மேற்கொள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். என்னை ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன். ☐

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளையும் மற்றும் சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக் கொள்ளவும் அதை பிரசுரிக்கவும் என் முழு மனதுடன் சம்மதிக்கிறேன். ☐

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன் எனக்கு கொடுக்கப்பட்ட அறிவுரைகளின்படி நடந்து கொள்வதுடன் இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதி அளிக்கிறேன். என் உடல்நலம் பாதிக்கப்பட்டாலோ அல்லது எதிர்பாராத வழக்கத்திற்கு மாறான நோய் குறி தென்பட்டாலோ உடனே அதனை மருத்துவ அணிக்கு தெரிவிப்பேன் என உறுதி அளிக்கிறேன். ☐

நோயாளியின் கையொப்பம் ..... இடம் ..... தேதி

கட்டைவிரல் ரேகை (இந்த படிவம் படித்து காட்டப்பட்டு புரிந்து கைரேகை அளிக்கின்றேன்)

பங்கு பெறுபவரின் பெயர் மற்றும் விலாசம் .....

.....

ஆய்வாளரின் கையொப்பம் ..... இடம் ..... தேதி

ஆய்வாளரின் பெயர் .....

PROFORMA

- S.no Date
- Age
- IP no
- Name
- Sex
- Unit
- Phone no.
- Address
- occupation
- Education
- Income

Presenting complaints:

jaundice / leg swelling / altered sensorium/fever/abdominal pain

Past history:

DM/HT/PT/SEIZURES/jaundice

Personal history:

smoking/alcoholism

Examination:

Pulse- BP-

RR-

CVS:

RS:

CNS:

Abdomen:

Investigations:

CBC:

Hb-

Pcv-

TC-

DC-

RFT:

Sugar-

Urea-

Creatinine-

LFT:

AST-

ALT-

S.Bilirubin-

s. protein-

s. albumin-

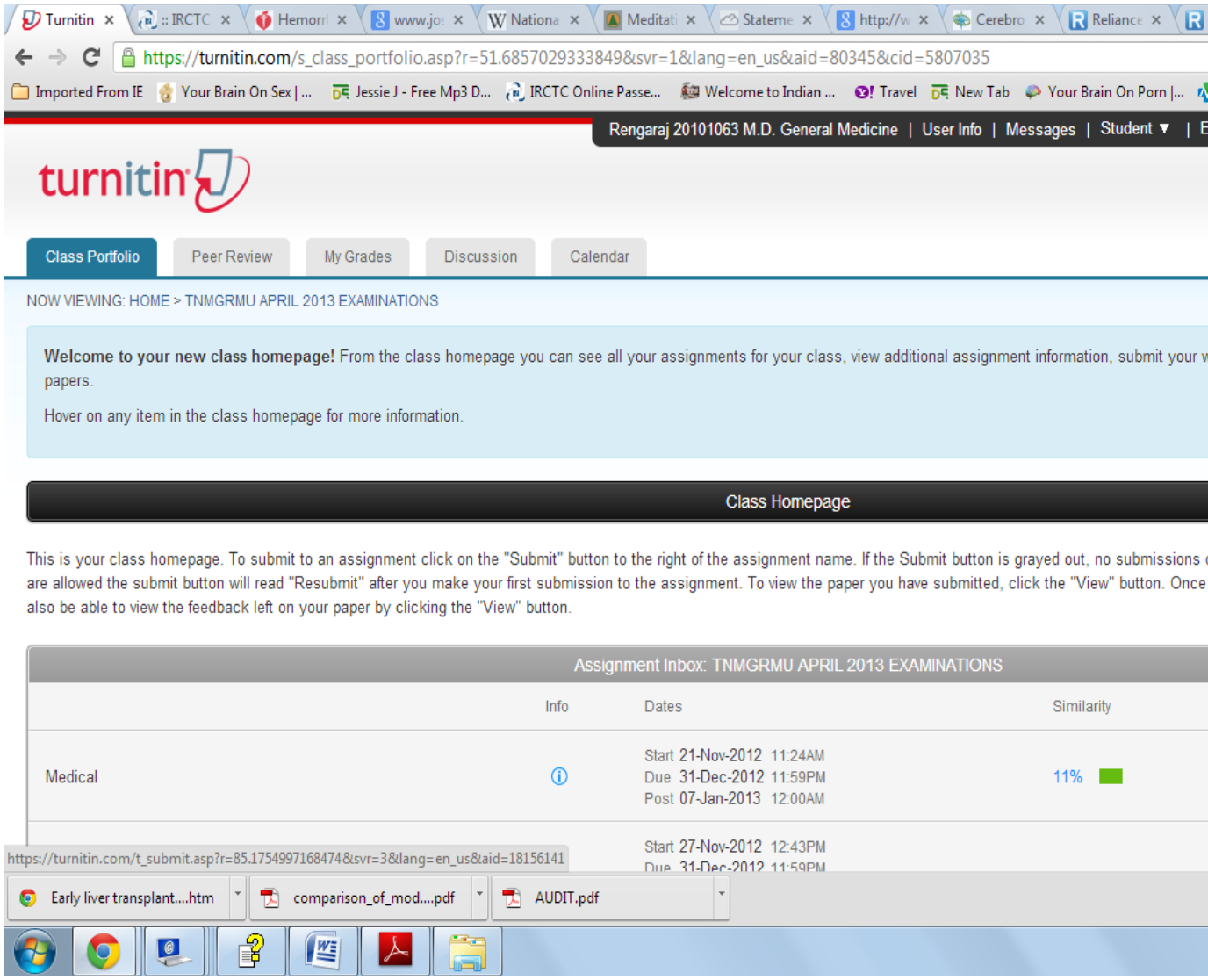
GGT-

SAP-

PT/INR-

USG abdomen:

name	age	sex	WCC	Urea	total bilir	SGOT	SGPT	PT	INR	m DF	GAHS	1 month m
mani	52	m	4200	22	11.4	245	234	18	1.5	43.6	8	survived
jayakuma	37	m	10100	24	5.4	176	98	16	1.4	23.8	5	survived
nagarathn	47	m	17400	17.5	17.3	257	212	18	1.5	44.9	9	death
silambara	43	m	6300	35	9.6	193	155	15	1.3	23.4	6	survived
raja	39	m	15500	45	7.8	327	261	18	1.5	35.4	9	death
tamizhara	26	m	4900	28	6.5	246	194	16	1.4	24.9	5	survived
ravi	49	m	27500	46	29.4	279	231	22	1.8	75.4	10	death
kunjithapa	40	m	12400	52	9.1	293	178	15	1.3	22.9	7	survived
boopathy	39	m	4700	24	5	228	159	22	1.8	51	7	survived
rajarajan	52	m	8700	41	8.7	323	215	17	1.5	31.7	8	death
sripathy	33	m	5600	30	10.6	236	163	16	1.4	29	7	survived
loger	28	m	12100	16	17	168	149	20	1.7	53.8	8	survived
raghu	56	m	17600	54	16	285	127	17	1.5	39	10	death
kalivaradh	31	m	9300	27	8.9	156	113	17	1.5	31.9	6	survived
balakrishr	52	m	8200	43	8.6	297	166	19	1.6	40.8	9	survived
rajamoort	25	m	7700	19	7.3	254	202	16	1.4	25.7	5	survived
sudakar	34	m	16600	40	15.8	325	176	16	1.4	34.2	9	death
anandan	46	m	12300	42	12.1	269	145	17	1.5	35.1	8	survived
ravikumar	43	m	8100	44	6.1	137	97	15	1.3	19.9	6	survived
krishnasar	47	m	7500	31	5.9	183	145	17	1.5	28.9	6	survived
maduraive	38	m	12600	38	7.8	281	240	16	1.4	26.2	7	survived
shanmuga	44	m	10500	26	8.3	195	108	17	1.5	31.3	6	survived
kannaih	35	m	18600	36	9.6	190	153	19	1.6	41.8	9	death
mannar	56	m	15300	31	10.9	327	198	16	1.4	29.3	9	death
narayanas	34	m	7400	29	9.9	241	119	16	1.4	28.3	6	survived
jagadeesa	48	m	6500	33	6.8	148	114	15	1.3	20.6	6	survived
kuppusam	43	m	9300	23	12.3	165	104	21	1.7	53.7	7	survived
david	51	m	8300	37	5.7	179	142	17	1.5	28.7	7	survived
subraman	38	m	13800	26	10.1	165	139	19	1.6	42.3	7	survived
irudhayara	41	m	16300	37	17.3	217	126	18	1.5	44.9	9	death
pandian	34	m	11600	29	7.4	155	126	15	1.3	21.2	6	survived
rajakannu	42	m	9300	34	8.1	201	103	16	1.4	26.5	7	survived
panchacha	53	m	8300	44	12.6	176	117	19	1.6	44.8	9	death
ezhil	29	m	19700	34	9.6	194	133	22	1.8	51.6	9	survived
arokiyaraj	31	m	6400	26	5.7	160	104	17	1.5	28.7	5	survived
vinoth	26	m	5700	43	9.2	214	167	15	1.3	23	7	survived
balakottai	58	m	17800	37	8.1	146	111	16	1.4	26.5	9	death
sureshkur	47	m	8400	38	10.6	143	84	16	1.4	29	7	survived
palani	39	m	9900	51	8.3	128	103	17	1.5	31.3	7	survived
sugumar	45	m	12800	16	9.7	186	140	16	1.4	28.1	6	survived
fazil	44	m	13200	28	9.3	122	101	21	1.7	50.7	7	survived
arjunan	41	m	18500	35	11.5	139	94	19	1.6	42.7	9	death
abdul kud	31	m	7900	38	10.5	152	123	19	1.6	42.7	7	survived
diwakar	28	m	4300	27	6.8	141	88	17	1.5	29.8	5	survived
sivakumar	40	m	5600	37	11.3	175	139	15	1.3	24.1	7	survived
munusam	46	m	16900	43	11.8	206	164	18	1.5	39.4	9	death
lingam	33	m	12600	38	15.4	173	129	23	1.9	66	9	death
srinivasan	37	m	8800	23	6.9	238	154	16	1.4	25.3	5	survived
kumarasa	62	m	11100	35	8.6	177	132	19	1.6	40.8	10	death
rajendran	27	m	6700	38	10.5	235	146	19	1.6	42.7	7	survived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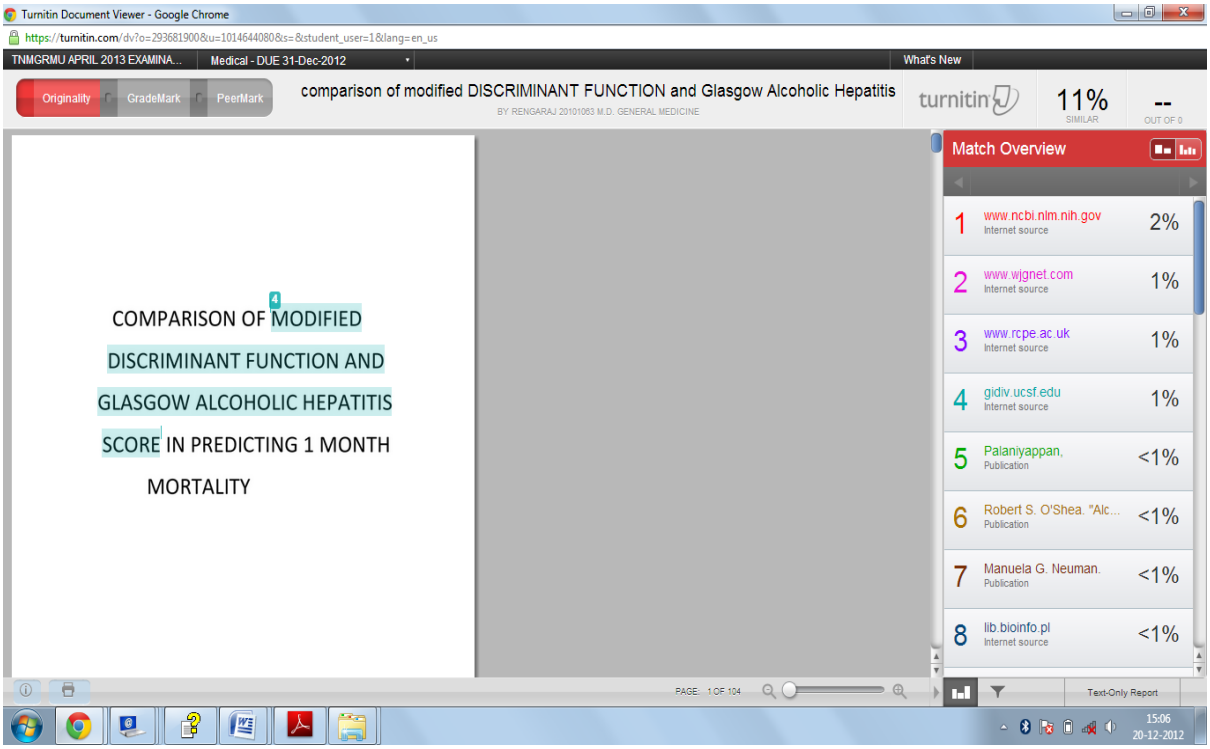
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